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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|--|-------------|----------------------|---------------------|------------------|
| 09/148,234 | 09/04/1998 | IOANNIS MOUTSATSOS | GI5298A | 3002 |
| 27130 | 7590 | 04/04/2006 | EXAMINER | |
| EITAN, PEARL, LATZER & COHEN ZEDEK LLP 10 ROCKEFELLER PLAZA, SUITE 1001 NEW YORK, NY 10020 | | | RIGGINS, PATRICK S | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1633 | |

DATE MAILED: 04/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|------------------------|---------------------|--|
| Office Action Summary | Application No. | Applicant(s) | |
| | 09/148,234 | MOUTSATSOS ET AL. | |
| | Examiner | Art Unit | |
| | Patrick S. Riggins | 1633 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 January 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 24-28 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 24-28 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Receipt is acknowledged of an amendment filed 1/19/06. Claims 24-28 are pending and under examination.
2. Receipt is also acknowledged of a request for interview received 2/15/06. Due to time constraints an interview could not be granted at the present time. If desired, Applicant is invited to request an interview after consideration of the Office Action below.

Claim Rejections - 35 USC § 103

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
4. Claims 24-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ahrens (DNA Cell Biol. 12:871-880 (1993), of record) in view of U.S. Patent No. 5,763,416 (hereinafter Bonadio, of record) and U.S. Patent No. 6,048,964 (hereinafter Lee, of record). The grounds for this rejection are maintained for the reasons of record in the previous office actions mailed 5/21/03, 6/15/04, and 7/21/05.
5. Claims 24-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ahrens, Bonadio, and Lee as applied to claims 24-26 above, and further in view of U.S. Patent No. 6,291,206 (hereinafter Wozney, of record). The grounds for this rejection are maintained for the reasons of record in the previous office actions filed 5/21/03, 6/15/04, and 7/21/05.
6. Claims 24-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ahrens, Bonadio, Lee, and Wozney as applied to claims 24-27 above, and further in view of U.S. Patent

No. 5,700,774 (hereinafter Hattersley, of record). The grounds for this rejection are maintained for the reasons of record in the previous office actions filed 5/21/03, 6/15/04, and 7/21/05.

Response to Arguments

7. Applicant's arguments filed 1/19/06 have been fully considered but they are not persuasive. Applicant simply rehashes the points that have been argued over time. Examiner stands by the previous arguments presented in the Office Actions mailed 5/21/03, 6/15/04, and 7/21/05. Applicant's main point of contention is that organized bone formation is an unexpected result achieved only using the methods of the instant application.

8. In short, this is irrelevant. Any added "unexpected" benefit which may arise from the practice of the claimed invention, is an inherent benefit of the claimed methods. In order for the art of record to render the instant claims obvious, the art of record only needs to provide a motivation to induce bone formation at a site of bone infirmity using the method of the claimed invention. The art of record indeed provides that motivation. The result that the bone formation is organized is irrelevant as this is simply a result of practicing an obvious method.

9. To ensure clarity, the original rejection over Ahrens, Bonadio, and Lee is reiterated hereinbelow.

10. Ahrens teaches at the abstract and materials and methods the *in vitro* transformation of a pluripotent stem cell with DNA encoding BMP-2 protein to study BMP-induced osteogenesis *in vitro*. Ahrens discusses the use of the transformed stem cells in treatment of a bone infirmity (see the introduction and page 879).

11. Ahrens does not teach the transformation of a human progenitor cell with BMP-2, nor the specific use of BMP-2 transformed cells to treat bone infirmity.

12. Bonadio teaches at columns 3-9 a method for producing cells for implantation at a site of a bone infirmity in a human (see especially column 5, lines 1-18, regarding *ex vivo* protocols) by transforming a cultured human progenitor cell or a bone marrow stromal cell with a DNA encoding bone morphogenesis protein 2(BMP-2) (column 6, line 63-column 7, line 29), then implanting the transformed cell into a site of bone infirmity. The cells may be pluripotent progenitor stem cells, a cell line, or a primary cell (see column 4, lines 32-67). Bonadio discusses the affect of BMP on bone formation, and recites the interaction of cells with are “responsive” to BMPs, as well as the intercellular “communication” of cells via bioactive BMP molecules. The need for BMP receptors in “responsive” cells is therefore implied.

13. Lee teaches at the claims, the use of BMP-2 to treat bone infirmity by directly introducing the protein into the site of the bone infirmity.

14. It would have been obvious to one of ordinary skill in the art at the time of the invention was made to modify the method of transforming a pluripotent stem cell *in vitro* with a DNA encoding DMP-2 protein as taught by Ahrens to produce a BMP-2 transformed human mesenchymal progenitor cell *ex vivo* which may then be introduced into a site of bone infirmity to treat a bone tissue of skeletal defect as taught by Bonadio, where Lee teaches the usefulness of treating a site of bone infirmity with recombinant BMP-2 protein to produce the instant claimed method because Ahrens teaches the practicality and feasibility of transforming a pluripotent stem cell with a DNA encoding BMP-2 *in vitro*, where Bonadio teaches the usefulness of the transformed pluripotent stem cell in a method of treating a site of a bone infirmity, and because

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Lee teaches the practicality and feasibility of treating bone infirmity by introducing recombinant BMP-2 protein to a site of bone infirmity. Bonadio specifically teaches the desirability of delivery of a pluripotent stem cell transformed *ex vivo* with DNA encoding BMP-2 protein to a site of a bone infirmity in a method of treatment of the bone infirmity by inducing osteogenesis at the site of the bone infirmity. Ahrens teaches that the transformation of cells with DNA encoding BMP-2 can be done, and Lee teaches that delivery of recombinant BMP-2 to cells at a site of bone infirmity will induce bone regeneration. Therefore, it would have been obvious to one of ordinary skill in the art that the combination of the teachings of Ahrens and Lee provides the reasonable assurance that the method of *ex vivo* implanting of the pluripotent transformed cells as taught by Bonadio would be successful for the expected benefit of treating a bone infirmity by regenerating bone tissue.

15. From this reiteration of the original rejection in the Office Action mailed 5/21/03, it is clear that motivation to combine Ahrens, Bonadio, and Lee has been provided for the treatment of a bone infirmity. The combined method of Ahrens, Bonadio, and Lee thus renders the instantly pending claims obvious.

Conclusion

16. No claim is allowed.

17. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

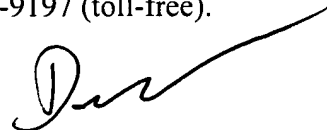
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MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick S. Riggins whose telephone number is (571) 272-6102. The examiner can normally be reached on M-F 7:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave T. Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Patrick Riggins, Ph.D.
Examiner
Art Unit 1633

DAVE TRONG NGUYEN
SUPERVISORY PATENT EXAMINER